

1/23

```
GAATTCGGCTTCCATCCTAATACGACTCACTATAGGGCTCGAGCGGCCCGCCGGGCGAGGTATCTTGGCTCACAGGGGA 79
M S S S S W L L L S L V A V T A A O S 19
CG ATG TCA AGC TCT TCC TGG CTC CTT CTC AGC CTT GTT GCT GTA ACT GCT GCT CAG TCC 138
T I E E Q A K T F L D K F N H E A E D L 39
ACC ATT GAG GAA CAG GCC AAG ACA TTT TTG GAC AAG TTT AAC CAC GAA GCC GAA GAC CTG 198
F Y Q S S L A S W N Y N T N I T E E N V 59
TTC TAT CAA AGT TCA CTT GCT TCT TGG AAT TAT AAC ACC AAT ATT ACT GAA GAG AAT GTC 258
Q N M N N A G D K W S A F L K E Q S T L 79
CAA AAC ATG AAT AAT GCT GGG GAC AAA TGG TCT GCC TTT TTA AAG GAA CAG TCC ACA CTT 318
A Q M Y P L Q E I Q N L T V K L Q L Q A 99
GCC CAA ATG TAT CCA CTA CAA GAA ATT CAG AAT CTC ACA GTC AAG CTT CAG CTG CAG GCT 378
L Q Q N G S S V L S E D K S K R L N T I 119
CTT CAG CAA AAT GGG TCT TCA GTG CTC TCA GAA GAC AAG AGC AAA CGG TTG AAC ACA ATT 438
L N T M S T I Y S T G K V C N P D N P Q 139
CTA AAT ACA ATG AGC ACC ATC TAC AGT ACT GGA AAA GTT TGT AAT CCA GAT AAT CCA CAA 498
E C L L L E P G L N E I M A N S L D Y N 159
GAA TGC TTA TTA CTT GAA CCA GGT TTG AAT GAA ATA ATG GCA AAC AGT TTA GAC TAC AAT 558
E R L W A W E S W R S E V G K Q L R P L 179
GAG AGG CTG TGG GCT TGG GAA AGC TGG AGA TCT GAG GTC GGC AAG CAG CTG AGG CCA TTA 618
Y E E Y V V L K N E M A R A N H Y E D Y 199
TAT GAA GAG TAT GTG GTC TTG AAA AAT GAG ATG GCA AGA GCA AAT CAT TAT GAG GAC TAT 678
G D Y W R G D Y E V N G V D G Y D Y S R 219
GGG GAT TAT TGG AGA GGA GAC TAT GAA GTA AAT GGG GTA GAT GGC TAT GAC TAC AGC CGC 738
G Q L I E D V E H T F E E I K P L Y E H 239
GGC CAG TTG ATT GAA GAT GTG GAA CAT ACC TTT GAA GAG ATT AAA CCA TTA TAT GAA CAT 798
L H A Y V R A K L M N A Y P S Y I S P I 259
CTT CAT GCC TAT GTG AGG GCA AAG TTG ATG AAT GCC TAT CCT TCC TAT ATC AGT CCA ATT 858
G C L P A H L L G D M W G R F W T N L Y 279
GGA TGC CTC CCT GCT CAT TTG CTT GGT GAT ATG TGG GGT AGA TTT TGG ACA AAT CTG TAC 918
S L T V P F G Q K P N I D V T D A M V D 299
TCT TTG ACA GTT CCC TTT GGA CAG AAA CCA AAC ATA GAT GTT ACT GAT GCA ATG GTG GAC 978
Q A W D A Q R I F K E A E K F F V S V G 319
CAG GCC TGG GAT GCA CAG AGA ATA TTC AAG GAG GCC GAG AAG TTC TTT GTA TCT GTT GGT 1038
L P N M T Q G F W E N S M L T D P G N V 339
CTT CCT AAT ATG ACT CAA GGA TTC TGG GAA AAT TCC ATG CTA ACG GAC CCA GGA AAT GTT 1098
Q K A V C H P T A W D L G K G D F R I L 359
CAG AAA GCA GTC TGC CAT CCC ACA GCT TGG GAC CTG GGG AAG GGC GAC TTC AGG ATC CTT 1158
M C T K V T M D D F L T A H H E M G H I 379
ATG TGC ACA AAG GTG ACA ATG GAC GAC TTC CTG ACA GCT CAT CAT GAG ATG GGG CAT ATC 1218 ZBD
Q Y D M A Y A A Q P F T L R N G A N E G 399
CAG TAT GAT ATG GCA TAT GCT GCA CAA CCT TTT CTG CTA AGA AAT GGA GCT AAT GAA GGA 1278
F H E A V G E I M S L S A A T P K H L K 419
TTC CAT GAA GCT GTT GGG GAA ATC ATG TCA CTT TCT GCA GCC ACA CCT AAG CAT TTA AAA 1338
S I G L L S P D F Q E D N E T E I N F L 439
TCC ATT GGT CTT CTG TCA CCC GAT TTT CAA GAA GAC AAT GAA ACA GAA ATA AAC TTC CTG 1398
L K Q A L T I V G T L P F T Y M L E K W 459
CTC AAA CAA GCA CTC ACG ATT GTT GGG ACT CTG CCA TTT ACT TAC ATG TTA GAG AAG TGG 1458
R W M V F K G E I P K D Q W M K K W W E 479
AGG TGG ATG GTC TTT AAA GGG GAA ATT CCC AAA GAC CAG TGG ATG AAA AAG TGG TGG GAG 1518
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Fig. 1A

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M K R E I V G V V E P V P H D E T Y C D 499
ATG AAG CGA GAG ATA GTT GGG GTG GTG GAA CCT GTG CCC CAT GAT GAA ACA TAC TGT GAC 1578
P A S L F H V S N D Y S F I R Y Y T R T 519
CCC GCA TCT CTG TTC CAT GTT TCT AAT GAT TAC TCA TTC ATT CGA TAT TAC ACA AGG ACC 1638
L Y Q F Q F Q E A L C Q A A K H E G F L 539
CTT TAC CAA TTC CAG TTT CAA GAA GCA CTT TGT CAA GCA GCT AAA CAT GAA GGC CCT CTG 1698
H K C D I S N S T E A G Q K L F N M L R 559
CAC AAA TGT GAC ATC TCA AAC TCT ACA GAA GCT GGA CAG AAA CTG TTC AAT ATG CTG AGG 1758
L G K S E P W T L A L E N V V G A K N M 579
CTT GGA AAA TCA GAA CCC TGG ACC CTA GAA AAT GTT GTA GGA GCA AAG AAC ATG 1818
N V R P L L N Y F E P L F T W L K D Q N 599
AAT GTA AGG CCA CTG CTC AAC TAC TTT GAG CCC TTA TTT ACC TGG CTG AAA GAC CAG AAC 1878
K N S F V G W S T D W S E Y A D Q S I K 619
AAG AAT TCT TTT GTG GGA TGG AGT ACC GAC TGG AGT CCA TAT GCA GAC CAA AGC ATC AAA 1938
V R I S L K S A L G D K A Y E W N D N E 639
GTG AGG ATA AGC CTA AAA TCA GCT CTT GGA GAT AAA GCA TAT GAA TGG AAC GAC AAT GAA 1998
M Y L F R S S V A Y A M R Q Y F L K V K 659
ATG TAC CTG TTC CGA TCA TCT GTT GCA TAT GCT ATG AGG CAG TAC TTT TTA AAA GTA AAA 2058
N O M I L F G E E D V R V A N L K P R I 679
AAT CAG ATG ATT CTT TTT GGG GAG GAG GAT GTG CGA GTG GCT AAT TTG AAA CCA AGA ATC 2118
S F N F F V T A P K N V S D I I F R T E 699
TCC TTT AAT TTC TTT GTC ACT GCA CCT AAA AAT GTG TCT GAT ATC ATT CCT AGA ACT GAA 2178
V E K A I R M S R S C R I N D A F R L N D 719
GTT GAA AAG GCC ATC AGG ATG TCC CGG AGC CGT ATC AAT GAT CCT TTC CGT CTG AAT GAC 2238
N S L E F L G I Q P T L G P P N Q P F V 739
AAC AGC CTA GAG TTT CTG GGG ATA CAG CCA ACA CTT GGA CCT CCT AAC CAG CCC CCT GTT 2298
S I W L I V F G V V N G V I V V G I V I 759
TCC ATA TGG CTG ATT GTT TTT GGA GTT GTG ATG GGA GTG ATA GTG GTT GGC ATT GTC ATC 2358 TMD
L I F T G I R D R K K K N K A R S G E N 779
CTG ATC TTC ACT GGG ATC AGA GAT CGG AAG AAG AAA AAT AAA GCA AGA AGT GGA GAA AAT 2418
P Y A S I D I S K G E N N P G F Q N T D 799
CCT TAT GCC TCC ATC GAT ATT AGC AAA GGA GAA AAT AAT CCA GGA TTC CAA AAC ACT GAT 2478
D V Q T S F * 806
GAT GTT CAG ACC TCC TTT TAG 2499
AAAAATCATATGTTTTTCCTCTTGAGGTGATTTTGTGTATGTAAATGTTAATTTTCATGGTATAGAAAATATAAGATGAT 2578
AAAGATATCATTAATGTCAAACATGACTCTGTTTCAGAAAAAAATGTCGAAAGACAACATGGCCAAGGAGAGAGC 2657
ATCTTCATTGACATTTGCTTTTCAGTATTTATTTCTGTCTCTGGATTGACTTCTGTTCTGTTTCTTAATAAGGATTTTGT 2736
ATTAGAGTATATTAGGGAAAGTGTGTATTTGGTCTCACAGGCTGTTTCAGGGATAATCTAAATGTAAATGTCTGTTGAAT 2815
TTCTGAAGTTGAAAAACAAGGATATATCATTTGGAGCAAGTGTGGATCTTGTATGGAATATGGATGGATCACTTGTAAGG 2894
ACAGTGCCCTGGGAACCTGGTGTAGCTGCAAGGATTGAGAATGGCATGCATTAGCTCACTTTTCATTTAATCCATTGTCAAG 2973
GATGACATGCTTTCTTCACAGTAACTCAGTTCAAGTACTATGGTGATTTGCCCTACAGTGATGTTTGGAAATCGATCATGC 3052
TTTCTTCAAGGTGACAGGTCTAAAGAGAGAAGAATCCAGGGAACAGGTAGAGGACATTGCTTTTTCACTTCCAAGGTGC 3131
TTGATCAACATCTCCCTGACAACACAAAACCTAGAGCCAGGGGCTCCCGTGAACCTCCAGAGCATGCCTGATAGAAATC 3210
ATTTCTACTGTTCTCTAACTGTGGAGTGAATGGAATTTCCAACGTATGTTCCACCTCTGAAGTGGGTACCCAGTCTCT 3289
TAAATCTTTTGTATTTGCTCACAGTGTGTTGAGCAGTGTGAGCACAAAGCAGACACTCAATAAATGCTAGATTTACACA 3368
CTCAAAAAAAAAAAAAAGGGCGGCCGC 3396

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Fig. 1B

3/23

ace-2 -----
hu-ACET -----
mu-ACET -----
rb-ACET -----
hu-ACE MGAASGRRGPGLLLLPLP-----LLLLL-PPQFALALDPGLQPGNFSADEAGAQLFAQSYN
mu-ACE MGAASGQGRGWPLSPPLLMLSLVLLQLP-SPAPA;DPGLQPGNFSPPDEAGAQLFAESYN
rat-ACE MGAASGQGRGWPLSPPLLMLSLVLLQLLPPSPAPALDPGLQPGNFSADEAGAQLFADSYN
rb-ACE MGAAPGRGRPRLLRPPPL-LLLLLLRPPPAALTLDPLGGLPGDFAADEAGARLFASSYN

ace-2 -----
hu-ACET -----
mu-ACET -----
rb-ACET -----
hu-ACE SSAEQVLFQSVAAASWAHDTNITAENARRQEEAALLSOFFAEWGOKAKELYEPWQNFDT
mu-ACE SSAEVVMFQSTVASWAHDTNITEENARRQEEAALVSOFFAEVWGKKAKELYESIWNFTD
rat-ACE SSAEVVMFQSTAASWAHDTNITEENARLQEEAALINQEFFAEVWGKKAKELYESIWNFTD
rb-ACE SSAEQVLFIRSTAASWAHDTNITAENARRQEEAALLSOFFAEWGRRLRSSMTRCGRTSFT

ace-2 -----
hu-ACET -----
mu-ACET -----
rb-ACET -----
hu-ACE POLRRIIGAVRTLGSANLPLAKRQOYNALLSNMSRIYSTAKVCLPNKTATCWSLDPDLTN
mu-ACE SKLRRIGSIRTGLPANLPLAQRRQOYNALLSNMSRIYSTGKVCFPNKATCWSLDPDLTN
rat-ACE QKLRRIGSVQTLGFANLPLTORLOYNALLSNMSRIYSTGKVCFPNKATCWSLDPDLTN
rb-ACE QSCAGSSGLCAFWPCQAP-GQAAADNSLLSNMSQIYSTGRSASPTPLPAAWSLDPDLNN

ace-2 -----
hu-ACET -----
mu-ACET -----
rb-ACET -----
hu-ACE ILASSRSYAMLLFAWEGWENNAAGIPLKPLYEDFTALSNEAYKQDGFDTGAYWRSWYNP
mu-ACE ILASSRSYAKLLFAWEGWHDVGIPLKPLYQDFTALSNEAYRQDDFSDTGAFWRSWYESP
rat-ACE ILASSRNYAKVLFWEGWHDVGIPLRPLYQDFTALSNEAYRQDGFSDTGAYWRSWYESP
rb-ACE ILASSRSYAMLLFAWEGWENAVGIPLKPLYQEFTALSNEAYRQDGFSDTGAYWRSWYDSP

ace-2 -----
hu-ACET -----
mu-ACET -----
rb-ACET -----
hu-ACE TFEDDLEHLYQOLEPLYLNLHAFVRRALHRRYGDRYINLRGPIPAHLLGDMWAQSWENIY
mu-ACE SFEESLEHLYHQLEPLYLNLHAYVRRALHRRYGDKYVNLRGPIPAHLLGDMWAQSWENIY
rat-ACE SFEESLEHLYHQVEPLYLNLHAFVRRALHRRYGDKYINLRGPIPAHLLGDMWAQSWENIY
rb-ACE TFEDLERIYHQLEPLYLNLHAYVRRVLRHRRYGDRYINLRGPIPAHLLGNMWAQSWESIY

ace-2 -----
hu-ACET -----
mu-ACET -----
rb-ACET -----
hu-ACE DMVVPFPDKPNLDVTSTMLQOGWNATHMFRVAEEFFTSLELSPMPPEFWEGSMLEKPADG
mu-ACE DMVVPFPDKPNLDVTSTMVQKGWNATHMFRVSEEFFTSGLSPMPPEFWAESMLEKPTDG
rat-ACE DMVVPFPDKPNLDVTSTMVQKGWNATHMFRVAEEFFTSGLSPMPPEFWAESMLEKPADG
rb-ACE DMVVPFPDKPNLDVTSTMVQKGWNATHMFRVAEEFFTSGLSPMPPEFWAESMLEKPEDG

ace-2 -----
hu-ACET -----
mu-ACET -----
rb-ACET -----
hu-ACE REVVCHASAWDFYNRKDFRIKQCTRVTMDQLSTVHHEMGHVQYLYQYKDLFVSLRRGANP
mu-ACE REVVCHASAWDFYNRKDFRIKQCTRVTMEQLATVHHEMGHVQYLYQYKDLHVSLLRRGANP
rat-ACE REVVCHASAWDFYNRKDFRIKQCTRVTMDQLSTVHHEMGHVQYLYQYKDLHVSLLRRGANP
rb-ACE REVVCHASAWDFYNRKDFRIKQCTQVTMDQLSTVHHEMGHVQYLYQYKQDPVSLRR-ANP

Fig. 2A

Fig. 2C

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ace-2      LGDKAYEWNNDNEMYLFRRSSVAYAMRQYFLKVKNQMILFGEEDVRVANLKPRI SFNFFVTA
hu-ACET    LGWFPQYNWTPN-----
mu-ACET    LGWPEYNWAPN-----
rb-ACET    LGWFPQYTWTPN-----
hu-ACE     LGWFPQYNWTPN-----
mu-ACE     LGWPEYNWAPN-----
rat-ACE    LGWPEYTWTPN-----
rb-ACE     LGWFPQYTWTPN-----
           **      * * *

ace-2      PKNVSDIIPRTEVEKAIRMSRSRINDAFRLNDNSLEFLGIQPTLGPPNPPVSTWLVVFG TMD
hu-ACET    -----SARSE-----GPLPDSGRVS-----FLGLDLD---AQQARVGQWVLLFL
mu-ACET    -----TARAE-----GSTAESNRVN-----FLGLYLE---PQQARVGQWVLLFL
rb-ACET    -----SARSE-----GSLPDSGRVN-----FLGMNLD---AQQARVGQWVLLFL
hu-ACE     -----SARSE-----GPLPDSGRVS-----FLGLDLD---AQQARVGQWVLLFL
mu-ACE     -----TARAE-----GSTAESNRVN-----FLGLYLE---PQQARVGQWVLLFL
rat-ACE    -----TARAE-----GSLPESNRVN-----FLGMYLE---PQQARVGQWVLLFL
rb-ACE     -----SARSE-----GSLPDSGRVN-----FLGMNLD---AQQARVGQWVLLFL
           .*:      .   :: *:      ***:      .*: . * . *: : *

ace-2      VVMGVIVVGIVILIFTGIRDRKKKNKARSGENPYASIDISKGENNPGFONDDVQTSFN
hu-ACET    GIALLVATLGLSQRLFSIR-HRSLHRHSEHG-----PQFGSEVELRHS--
mu-ACET    GVALLVATVGLAHRLYNIRNHHSLRRPHRG-----PQFGSEVELRHS--
rb-ACET    GVALLLASLGLTQRLFSIR-YQSLRQPHHG-----PQFGSEVELRHS--
hu-ACE     GIALLVATLGLSQRLFSIR-HRSLHRHSEHG-----PQFGSEVELRHS--
mu-ACE     GVALLVATVGLAHRLYNIRNHHSLRRPHRG-----PQFGSEVELRHS--
rat-ACE    GVALLVATVGLAHRLYNIHNNHSLRRPHRG-----PQFGSEVELRHS--
rb-ACE     GVALLLASLGLTQRLFSIR-YQSLRQPHHG-----PQFGSEVELRHS--
           :   : :   :   : .*:   : . :   *           * * .   : : : *
```

Fig. 2D

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HUM_tACE -----
HUM_ACE MGAASGRGPGGLLLPLPLLLLLLPPQPALALDPGLQPGNFSADEAGAQLFAQSYNSSAEQV
DROME_ACE -----
ace-2 -----
CE_ACE -----

HUM_tACE -----
HUM_ACE LFQSVAAASWAHDTNITAENARRQEEAALLSQEFAEWGQKAKELYEPIWQNFTDPQLRRI
DROME_ACE -----
ace-2 -----
CE_ACE -----

HUM_tACE -----
HUM_ACE IGAVRTLGSANLPLAKRQQYNALLSNMSRIYSTAKVCLPNKTATCWSLDPDLTNILASSR
DROME_ACE -----
ace-2 -----
CE_ACE -----

HUM_tACE -----
HUM_ACE SYAMLLFAWEGWENNAAGIPLKPLYEDFTALSNEAYKQDGFTDTGAYWRSWYNSPTFEDDL
DROME_ACE -----
ace-2 -----
CE_ACE -----

HUM_tACE -----
HUM_ACE EHLVQQLLEPLYLNLHAFVRRALHRRYGDRIYNLRGPIPAHLLGDMWAQSWENIYDMVVPF
DROME_ACE -----
ace-2 -----
CE_ACE -----

HUM_tACE -----
HUM_ACE PDKPNLDVTSTMLQQGWNATHMFRVAEEFETSLELSPMPPEFWEGSMLEKPADGREVVCH
DROME_ACE -----
ace-2 -----
CE_ACE -----

HUM_tACE -----
HUM_ACE ASAWDFYNRKDFRIKQCTRVTMDQLSTVHHEMGHIQYYLQYKDLFVSLRRGANPGFHEAI
DROME_ACE -----
ace-2 -----
CE_ACE -----

HUM_tACE -----
HUM_ACE GDVLALSVATPEHLHKIGLLDRVTNDTESDINYLLKMALEKIAFLPFGYLVDQWRWGVFS
DROME_ACE -----
ace-2 -----
CE_ACE -----MKFHILLLLLV

HUM_tACE -----
HUM_ACE GRTPPSRYNFDWWYLRTKYQGICPPVTRNETHFDAGAKFHVPNVTPYIRYFVSVFLQFQF
DROME_ACE -----
ace-2 -----
CE_ACE GACLPVFTQEIKPPELLPADEAPKDPEAVFSEGEFFELTDALDTPKNGSVVPPEPEPKP

Fig. 3A

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```

HUM_tACE -----MGQGWATAGLPSLLFLLLCYGHPLL
HUM_ACE HEALCKEAGYEGPLHQCDIYRSTKAGAKLRKVLQAGSSRPWQEVLDKDMVGLDALDAQPLL
DROME_ACE -----
ace-2 -----
CE_ACE EPEPEPEPKPEPEPSPTPEPEPAIKFDNIESDYGDVAETAASTQPDENTEVIEQLVDT

HUM_tACE VPSQEASQQVTVTHGTSSQATTSSQTTTHQATAHOTSAQSPNLVTDEAEASKFVEEYDRT
HUM_ACE KYGQPVTVQWLQEQNQONGEVLGWPEYQWHPFLPDNYPEG-IDLVTDAAEASKFVEEYDRT
DROME_ACE -----MRLFLALLATLAVTQALVKEEIQAKEYLENLNKE
ace-2 -----MSSSSWLLLSLVAVTAAQSTIEEQAKTFLDKFNHE
CE_ACE FLNTGSIASNKTNRKGPVFANPVAQALVNSSNYWKTNDLQAPGSIKDEEKLRSWLAGYEA
          . * : :

HUM_tACE SQVVWNEYAEANWNYNTNITTTETSKILLQKNMQLANHTLKYGTQARKFDVNQLONTTIKR
HUM_ACE SQVVWNEYAEANWNYNTNITTTETSKILLQKNMQLANHTLKYGTQARKFDVNQLONTTIKR
DROME_ACE LAKRTNVETEAAWAYGSNITDENKKKNEISAEIAKFMKEVASDTTKQWF SYQSEDLR
ace-2 AEDLFYQSSLASWNYNTNITTEENVQNMNAGDKWSAFLKEQSTLAQMYPLQEIQLNLTVKL
CE_ACE AIKVLREVALSGWRYFNDASPSLKLALDAENVLTMTFVRSTSMQAKQFDMASVTDEKVMR
          : : * * . : : : : : : : : : : : : : : : :

HUM_tACE IIKKVQDLERAALPAQEELEFNKILLDMETTYSVATVCHPNGS---CLQLEPDLTNVMAT
HUM_ACE IIKKVQDLERAALPAQEELEFNKILLDMETTYSVATVCHPNGS---CLQLEPDLTNVMAT
DROME_ACE QFKALTGLGYAALPEDDYAELLDTLSAMESNFAKVVCYDKDSTKCDLALDPEIEEVISK
ace-2 QLQALQONGSSVLSSEDKSKRLNTILNMTSTIYSTGKVCNPDNPQE-CLLLEPGLNEIMAN
CE_ACE QLGYSFEGMSALAPSRFADYSQAQAALNRDSDKSTICDKDVPPP-CALQKIDMSIFRN
          : : : : * . : : : : : : : : : : : : : : : :

HUM_tACE SRKYEDLLWAWEGWRDKAGRAILOFYPKYVELINQAARLNGYVDAGDSWRSMYETP----
HUM_ACE SRKYEDLLWAWEGWRDKAGRAILOFYPKYVELINQAARLNGYVDAGDSWRSMYETP----
DROME_ACE SRDHEELAYYWREFYDKAGTAVRSQFERYVELNKAALNNFTSGAEAWLDEYEDD----
ace-2 SLDYNERLWAWESWRSEVVGKQLRPLYEYVVLKNEMARANHYEDYGDYWRGDIYVNGVDG
CE_ACE EKDASRLQHLWVSYVTAIAKSK-PSYNNITISNEGAKLNGFANGGAMWRSAPDMSS--K
          . . . * : : : : : : : : : : : : : : : :

HUM_tACE -----SLEQDLERLFOELQPLYLNLHAYVRRALHRHYG-AQHINLEGPIPAHLLGNMWA
HUM_ACE -----SLEQDLERLFOELQPLYLNLHAYVRRALHRHYG-AQHINLEGPIPAHLLGNMWA
DROME_ACE -----TFEQOLEDIFADIRPLQOIHGYVRFRLRKHYG-DAVVSSETGPIPMHLLGNMWA
ace-2 YDYSRGOLIEDVEHTFEETKPLYEHLHAYVRAKLNNAY--PSYISPIGCLPAHLLGDMWG
CE_ACE VHKAEDLNLKQIDKIYSTIQPFYQLLHAYMRRQLAGIYSNPFVGLSKDGPPIPAHLFGSLDG
          : : : : : : : : * * * * * : : * * * * : :

HUM_tACE QTWSNIYDLVVPFSA--PSMDTTEAMLKQGWTPRRMFKEADFFTSGLLPVPPEFWNK
HUM_ACE QTWSNIYDLVVPFSA--PSMDTTEAMLKQGWTPRRMFKEADFFTSGLLPVPPEFWNK
DROME_ACE QQWSEIADIVSPFPEK--PLVDVSAEMEKAQYTPKMFQMGDDFFTSNNLTKLQDFWDK
ace-2 RFWTNLYSLTVPGQK--PNIDVTDAVMDQAWDAQRIFKEAEKFFVSVGLPNMTQGFWEN
CE_ACE GDWSAHYEQTKPFEESETPAMLSAFTONTYTTKKMFVTAYRYFKSAGFPHLPKSYWTS
          * : : * * . : : : : : : : : : : : : : : : :

HUM_tACE SMLEKPTDGREVVCHAS-AWDFYNGKDFRIKQCTTVNLEDLVVAHHEMGHIQYFMQYKDL
HUM_ACE SMLEKPTDGREVVCHAS-AWDFYNGKDFRIKQCTTVNLEDLVVAHHEMGHIQYFMQYKDL
DROME_ACE SIIEKPTDGRDLVCHAS-AWDFYLLDDVRIKQCTRTVDQLFTVHHELGHQYFLQYQHQ
ace-2 SMLTDPGNVQKAVCHPT-AWDLGKG-DFRIIMCTKVMTDDFLTAHHEMGHIQYDMAYAAQ
CE_ACE SIFAR-VWSKDMICHAPAAALDMRAPNDFRVKACAQLGEPDFEQAHSLLVQTYQYLYKQD
          * : : : : * * : : * * : : : : : * : : *

HUM_tACE PVALREGANPGFHEAIGDVLALSVPSTPKHLSLNLSSSEGGSD--EHDINFLMKMALDKI
HUM_ACE PVALREGANPGFHEAIGDVLALSVPSTPKHLSLNLSSSEGGSD--EHDINFLMKMALDKI
DROME_ACE PFVYRTGANPGFHEAVGDVLSVSTPKHLEKIGLLKQYVRDD--EARINQLFLTALDKI
ace-2 PFLLRNGANEGFHEAVGEIMSLSATPKHLKLSIGLLSPDFQEDN-ETEINFLKQALTV
CE_ACE SLLFREQASPVITDAIANAFHLSLTPHYLYSQKLVPSHLDIKDSVIINKLYKESLESF
          . . * * . : : : : : : : : * : : . * * * : *

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Fig. 3B

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HUM_tACE AFIPFSYLVQDQWRWRVFDGSITKENYNQEWWSLRLKYQGLCPPVPRTQGDFFDPAKFHIP
HUM_ACE AFIPFSYLVQDQWRWRVFDGSITKENYNQEWWSLRLKYQGLCPPVPRTQGDFFDPAKFHIP
DROME_ACE VFLLPFAFTMDKYRWSLFRGEVDKANWNCAFWKLRDEYSGIEPPVVRSEKDFDAPAKYHIS
ace-2 GTLPFTYMLEKWRWMVFKGEIPKQDQWKKWEMKREIVGVVEPVPHDETYCDPASLHFVS
CE_ACE TKLPFTIAADNWRVYELFDGTVPKKNLDRWWEIRNKYEGVRSPPQPYNTSNLDALIHNSVS
      ***:   ::*:  * * : * :   :*:::  * : *   * .   :.

HUM_tACE -SSVPYIRYFVSFIIQFQFHEALCOAAGHTG-----PLHKCDIYQSKEAGQRLATAMKL
HUM_ACE -SSVPYIRYFVSFIIQFQFHEALCOAAGHTG-----PLHKCDIYQSKEAGQRLATAMKL
DROME_ACE -ADVEYLRYLVSFIIQFQFYKSACIKAGQYDPDNVELPLDNCDIYGSARAGAAFHNMILSM
ace-2 -NDYSFIRYYTRTLYQFQFQALCOAAKHG-----PLHKCDISNSTEAGQKLFNMLRL
CE_ACE QVHSPATRTLISYVLKFQILKALCQRELFWL-----SEGCTLSEDFT---EKLRETMKL
      *       : ***:  : *       .       :       : :

HUM_tACE GFSRPWPEAMQLITGQPNMSASAMLSYFKPLLDWLRTEN-----
HUM_ACE GFSRPWPEAMQLITGQPNMSASAMLSYFKPLLDWLRTEN-----
DROME_ACE GASKPWPDALEAFNGERIMSGKATAEYFEPLRVWLEAEN-----
ace-2 GKSEPWTALENVVGAKNMNVRPLLNYFEPLFTWLKDQNKNSFVGWSTDWSPYADQSIK
CE_ACE GSSITWLKALEMISGKGELDAQPLLEYEPLINWLRNFTN-----
      * * . * *: . *   :.   . : .*: ** . *

HUM_tACE -ELHGEKLGWPQYNWTPNSAR-----
HUM_ACE -ELHGEKLGWPQYNWTPNSAR-----
DROME_ACE -IKNNVHIGWTTSNKCVSS-----
ace-2 RISLKSALGDKAYEWNNDNEMYLFRSSVAYAMROYFLKVKNQMLFGEEDVRVANLKPRIS
CE_ACE -EIDQVVVGWDGEGTPTVEEIPKTRQPGDGGNGLPSEDVAFPGGE-----
      : *       .

HUM_tACE -----SEGPLPDSGRVSFLGLDLDAQQARVG-----Q
HUM_ACE -----SEGPLPDSGRVSFLGLDLDAQQARVG-----Q
DROME_ACE -----
ace-2 FNEFFVTAPKNVSDIIPRTEVEKAIRMSRSRINDAFRLNDNSLEFLGIQPTLGPPNQPPVS
CE_ACE -----CVNGQECLLDSHCNGTICVCNDGLYTFLEIGNTFN---CVPGN

HUM_tACE WLLLFLGIALLVATLGLSQRIFS-IRHR-----SLHRHSHGPGQFGSEVE
HUM_ACE WLLLFLGIALLVATLGLSQRIFS-IRHR-----SLHRHSHGPGQFGSEVE
DROME_ACE -----
ace-2 IWLIVFGVVMGVIVVGIVILIFTGIRDRKKKNKARSGENPYASIDISGENNPGFQNTDD TMD
CE_ACE PADSGFGDGKGLVIGLDFNNEVTTPESAEPEP---TAKTTTKMPPRVRAATSPFSLYLTV

HUM_tACE LRHS----
HUM_ACE LRHS----
DROME_ACE -----
ace-2 VQTSFN--
CE_ACE LLIIFYAL
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Fig. 3C

10/23

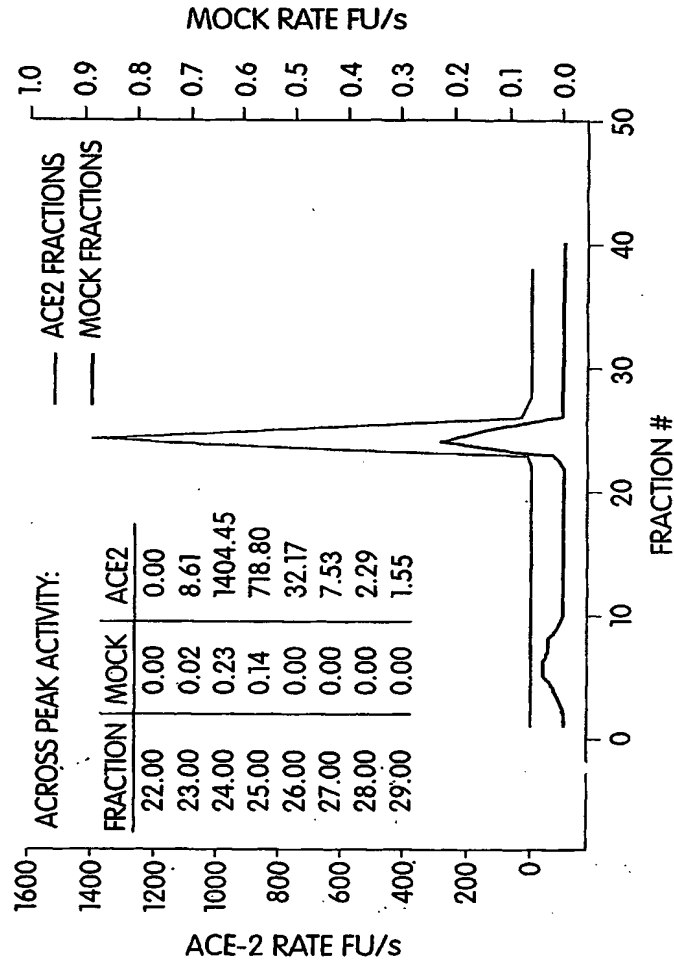


Fig. 4

11/23

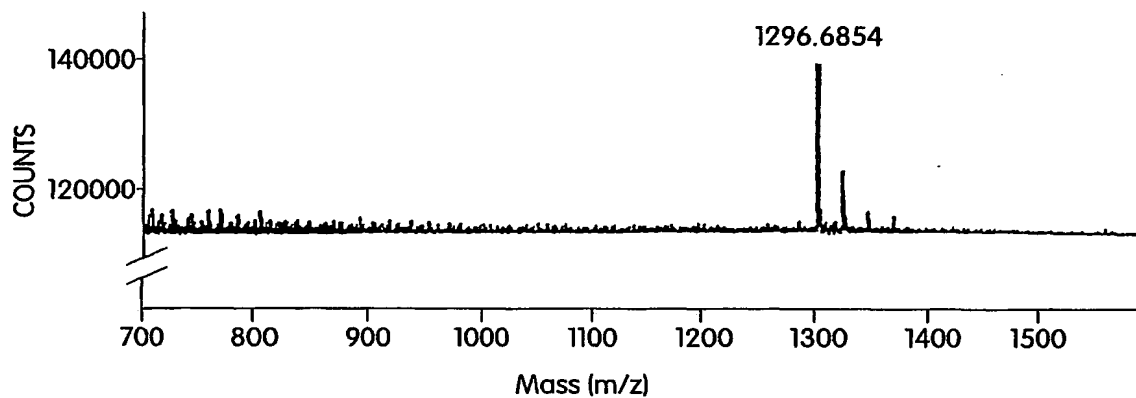


Fig. 5A

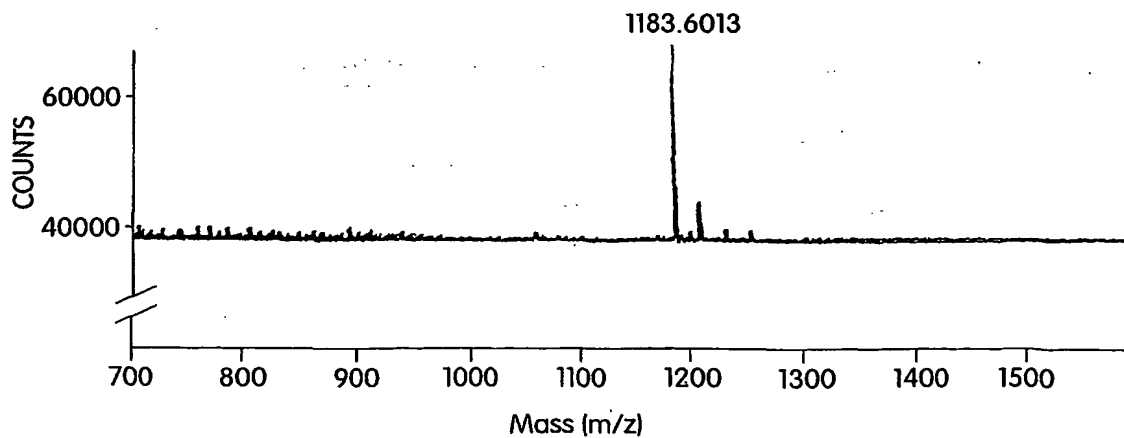


Fig. 5B

12/23

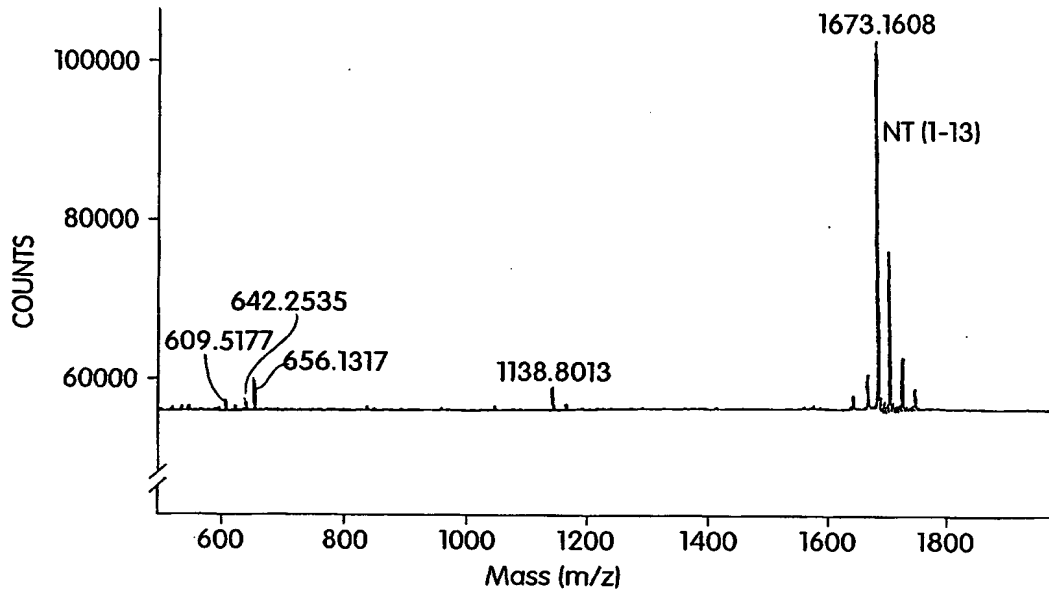


Fig. 6A

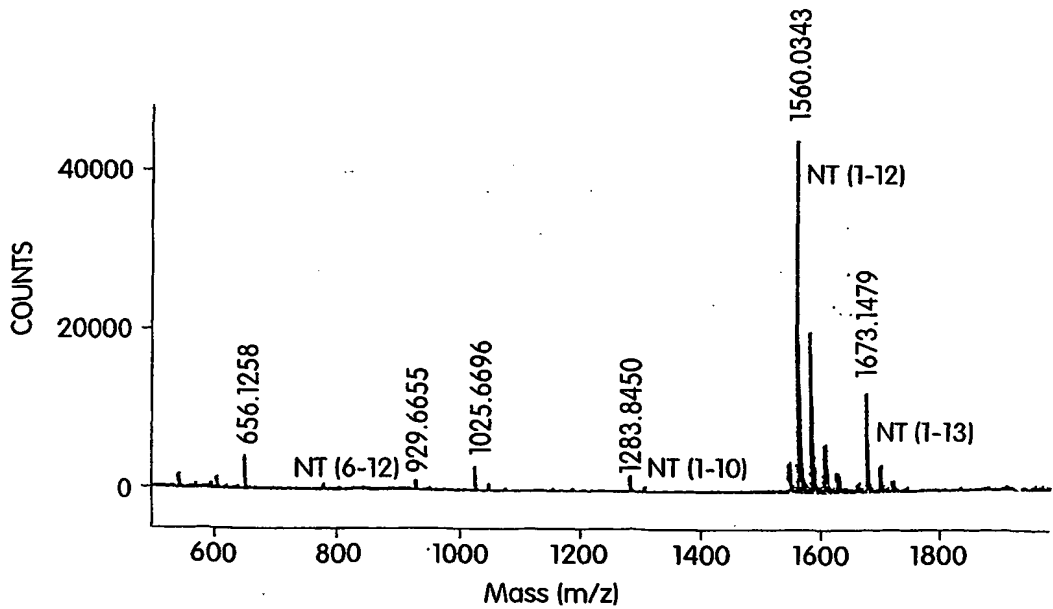


Fig. 6B

13/23

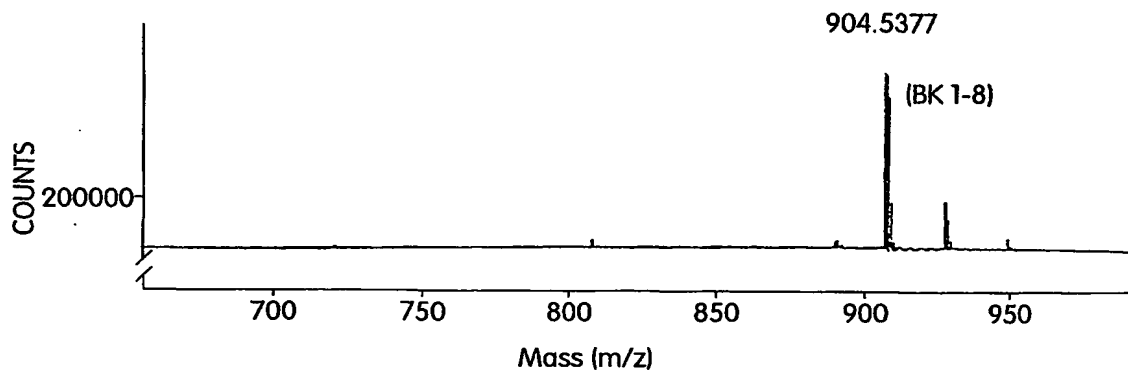


Fig. 7A

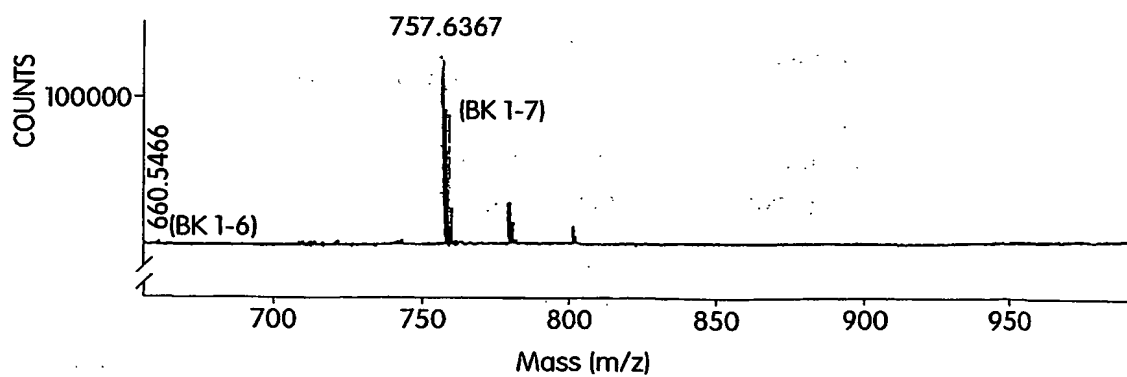


Fig. 7B

14/23

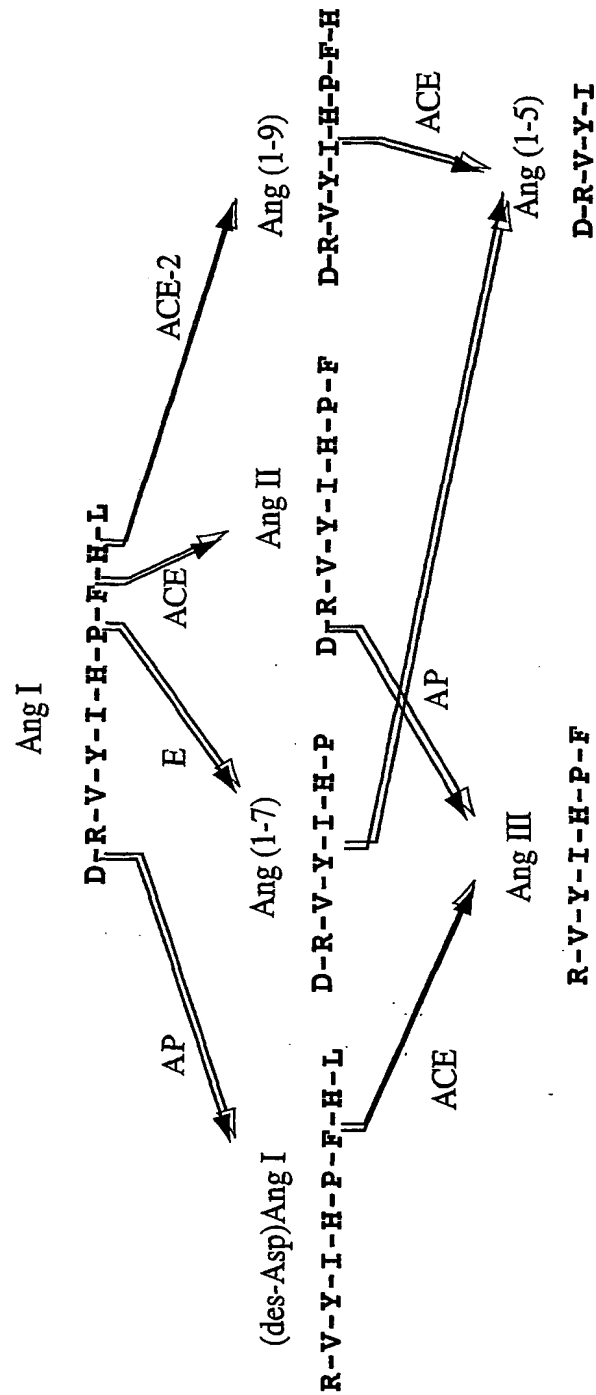


Fig. 8

15/23

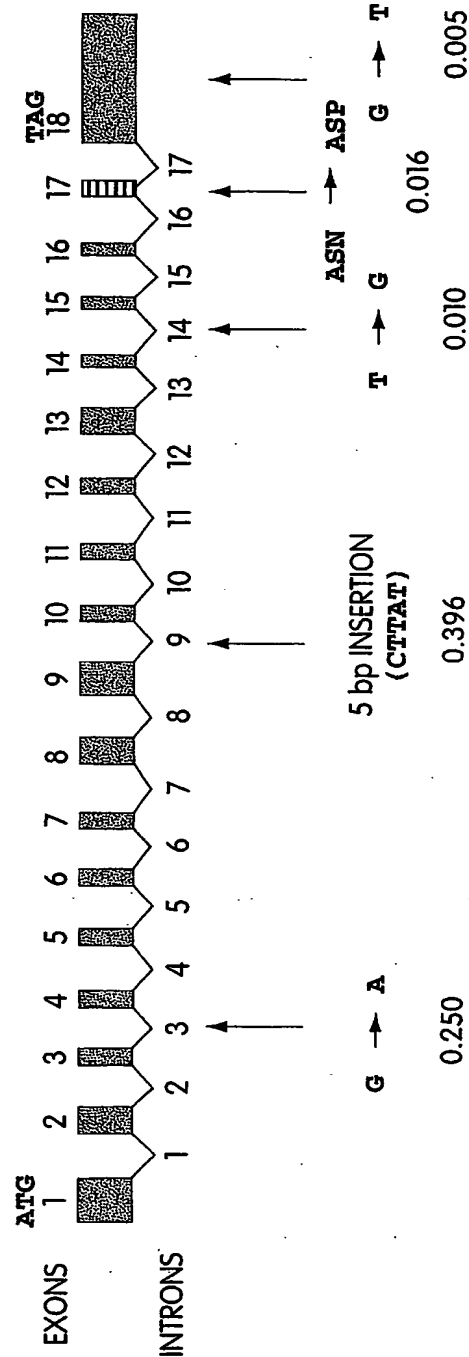


Fig. 9A

16/23

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CAGGAAGCCGAGACCTGTTCTATCAAGTTCACTTGTCTTCTGGAATTATAACACCAATATTACTGAAGAGATGTCCAAAACAT /
GAATAATGCTGGGGACAATGGTCTGCCCTTTTAAAGGAACAGTCCACACTTGGC
CAATATGATCCACTACAAGAAATTCAGAACTCAGAGTCAAGCTTCAGCTGCAGGCTCTTCAGCAAAATGGGTCTTCAGTGTCTCAGAA
GACAAGAGCAACCG / TTGAACACAATTTCTAAAT

G-A INTRONIC
3a/3b

ACAATGAGCACCATTCTACGACTGGAAGGTTTGTAAACCAGATAATCCACAAGAAATGCTTATTACTTGAACCAGG /
TTTGAATGAAATAATGGCAACAGTTTAGACTACAATGAGAGGCTCTGGGC
TTGGGAAAGCTGGAGATCTGAGGTCGGCAAGCAGCTGAGGCCATTATATGAGAGTATGTGGTCTTGAAAAATGAGATGGCAAGAGCAA
ATC / ATTATGAGGACTATGGGGATTATTGGAGAGGAG
ACTATGAAGTAAATGGGTAGATGGCTATGACTACAGCCGCGGCCAGTTGATTGAAGATGTGGAACATACCTTTGAAGAG /
ATTAAACCATTTATATGAACATCTTCATGCCCTATGTGAGGGC
AAAGTTGATGAATGCCATATCTTCTATATCACTCAATTTGGATGCCCTCCCTGCTCATTTGCTTGG /
TGATATGTGGGGTAGAATTTTGGACAATCTGTACTCTTTGACAGTTCCCTTTGGACAGAAA
CCAAACATCGATGTACTGATGCAATGGTGGACAG / GCCTGGGATGCACAGAGAAATATT
CAAGGAGGCCGAGAAGTTCTTTGTATCTGTTGGTCTTCTTAATATGACTCAAGGATTTCTGGGAAAATTCATGCTAACGGACCCAGGAAA
TGTTCAAGAAAGCAGTCTGCCATCCACAGCTTGGGACCTGGG /
GAAGGGCGACTTCAGGATCTTATGTGCACAAAGGTGACAAATGGAGCAGCTTCCTG
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5 bp INSERTION
(CTAT)

ACAATG / AAACAGAAATAAACTTCCTGCTCAAAACAGCACTCAGGATTTGTGGGACTCTGCCATTTACTTA
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GCTCACTACTTTGAGCCCTTATTTACCTGGCTGAAGACCAGAACAGAAATTTTGTGGGATGGAGTACCGACTGGAGTCC /
ATATGCAGACCAAGCATCAAGTGAGGATAAG

INTRONIC
9a/9b

CCTAAATCAGCTCTTGGAGATAAAGC / ATATGAATGGAACGACAAATGAAATGTACC
TGTTCGATCCTCTGTCATATGCTATGAGGCACTACTTTTAAAGTAAAAATCAGATGATCTTTTGGG /
GAGGAGGATGTGCGAGTGGCTAATTTGAACCAAGAAATCTCTTTAATTTCTTT
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GATTTACACATC / AAAAAAAAAAAAAAAAAAGGGCGGCGC

T-G INTRONIC
14a/14b

A-G ASN-ASP
17c/17d

G-T 3'UTR
18e/18f

Fig. 9B

17/23

Bachem M-2195
Mca-Tyr-Val-Ala-Asp-Ala-Pro-Lys(Dnp)-OH
Caspase I (ICE) substrate

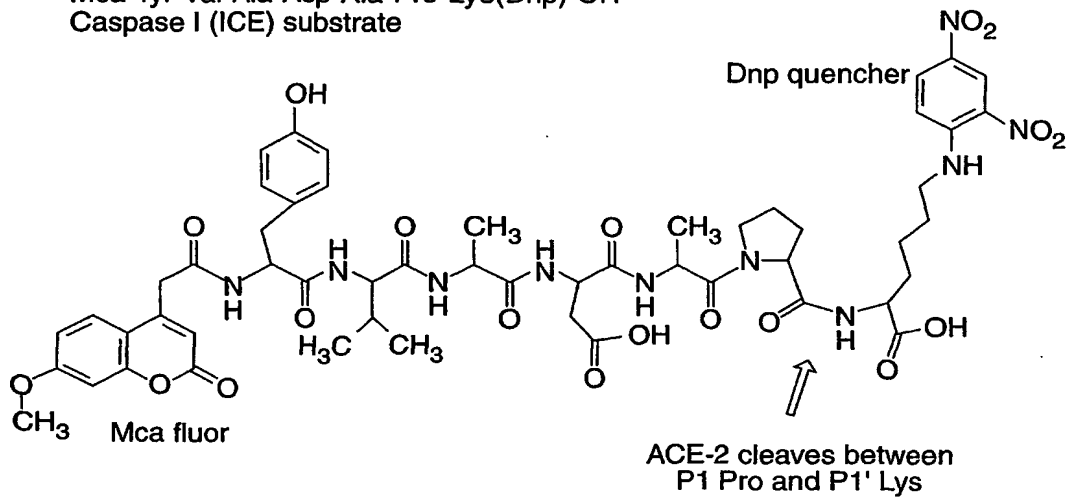


Fig. 10A

MIPH-1
custom synthesis (AnaSpec)
Mca-Ala-Pro-(Dnp)Lys-OH

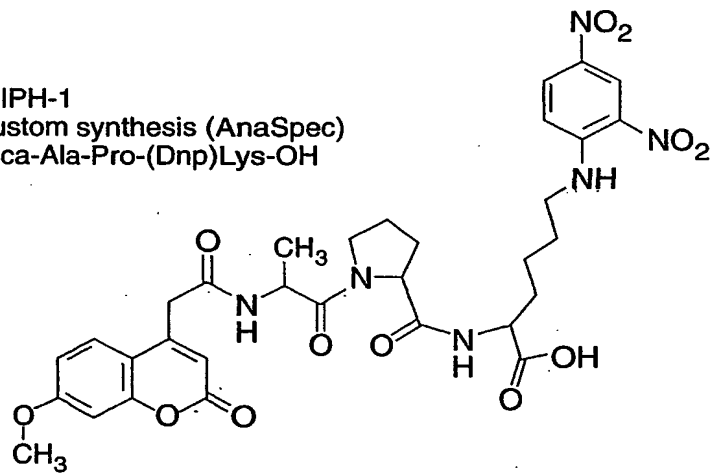


Fig. 10B

18/23

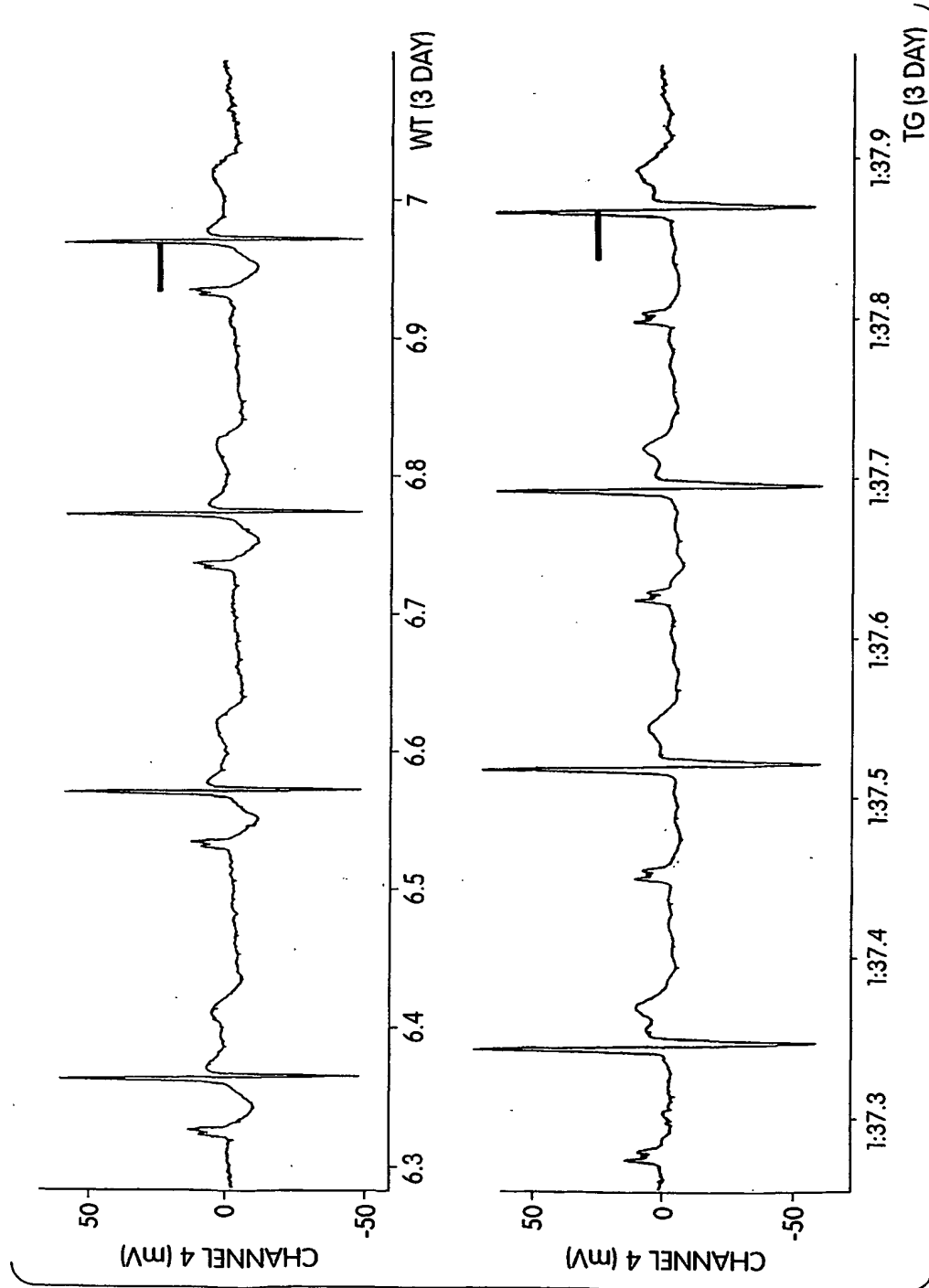


Fig. 11A

19/23

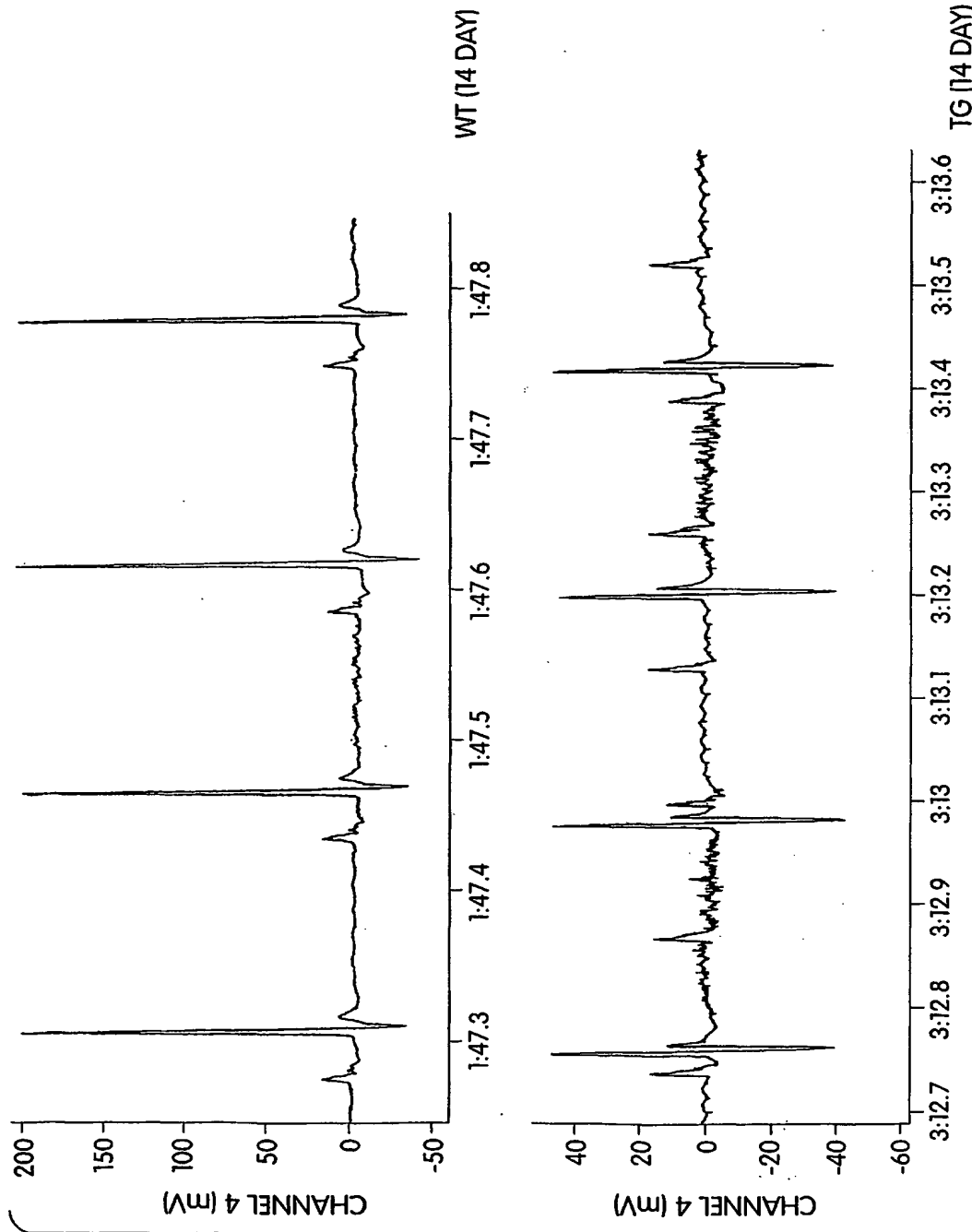


Fig. 11B

20/23

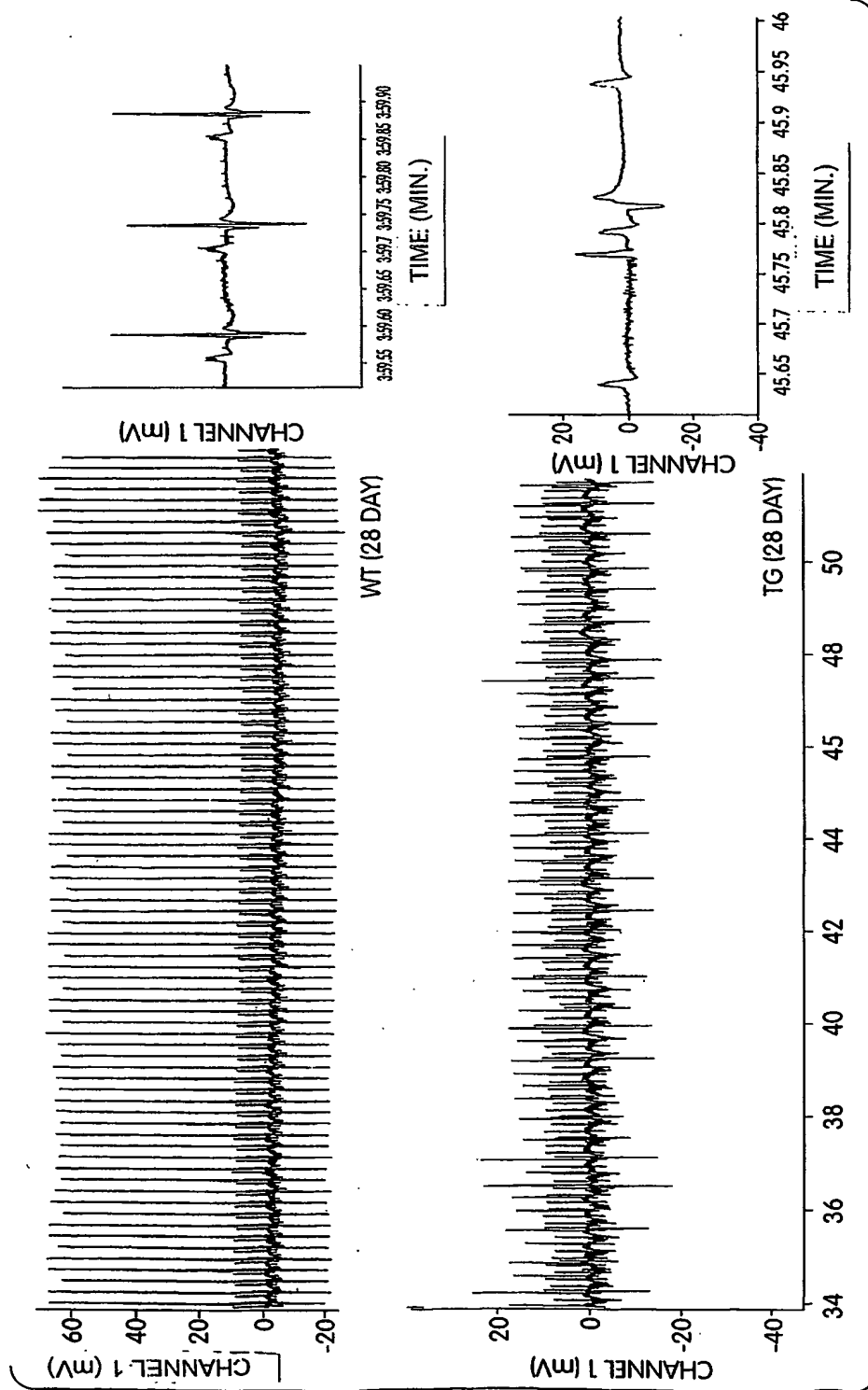
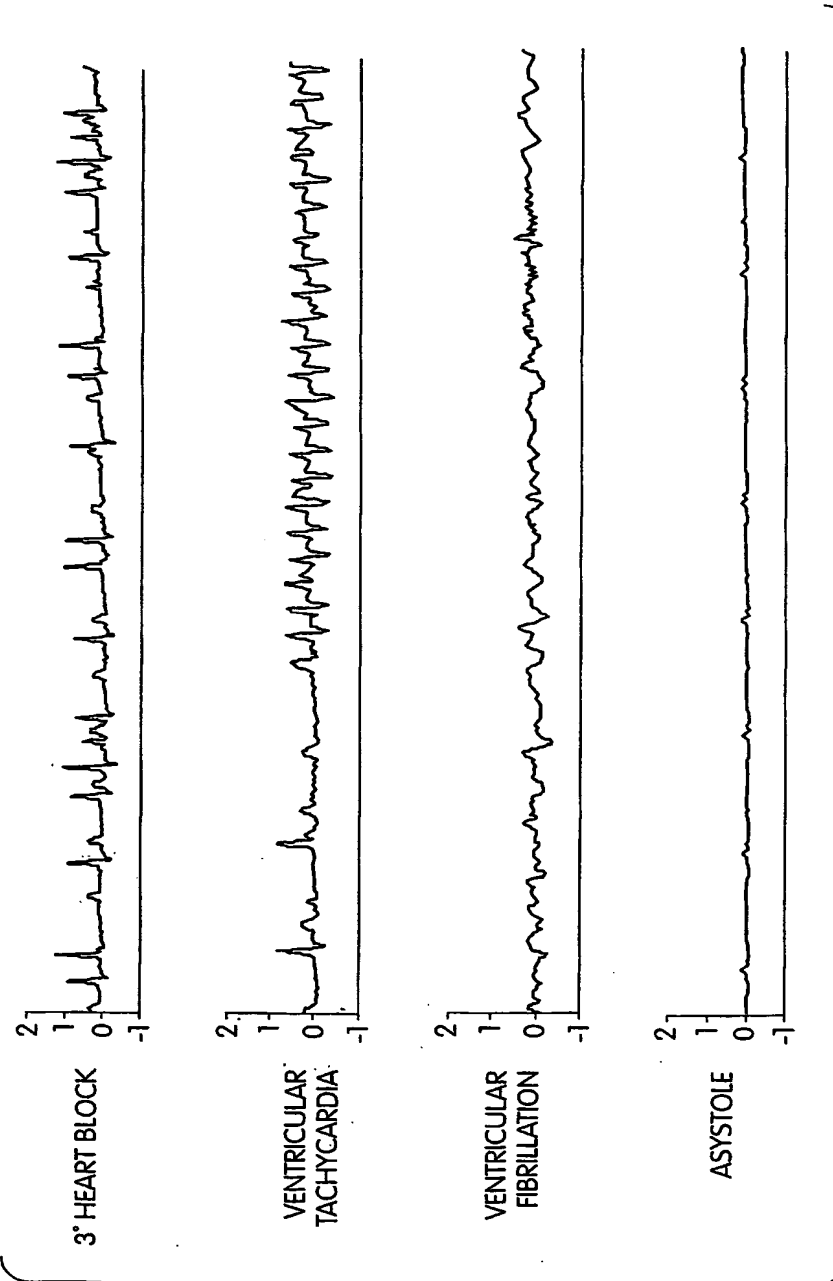


Fig. 11C

21/23



22/23

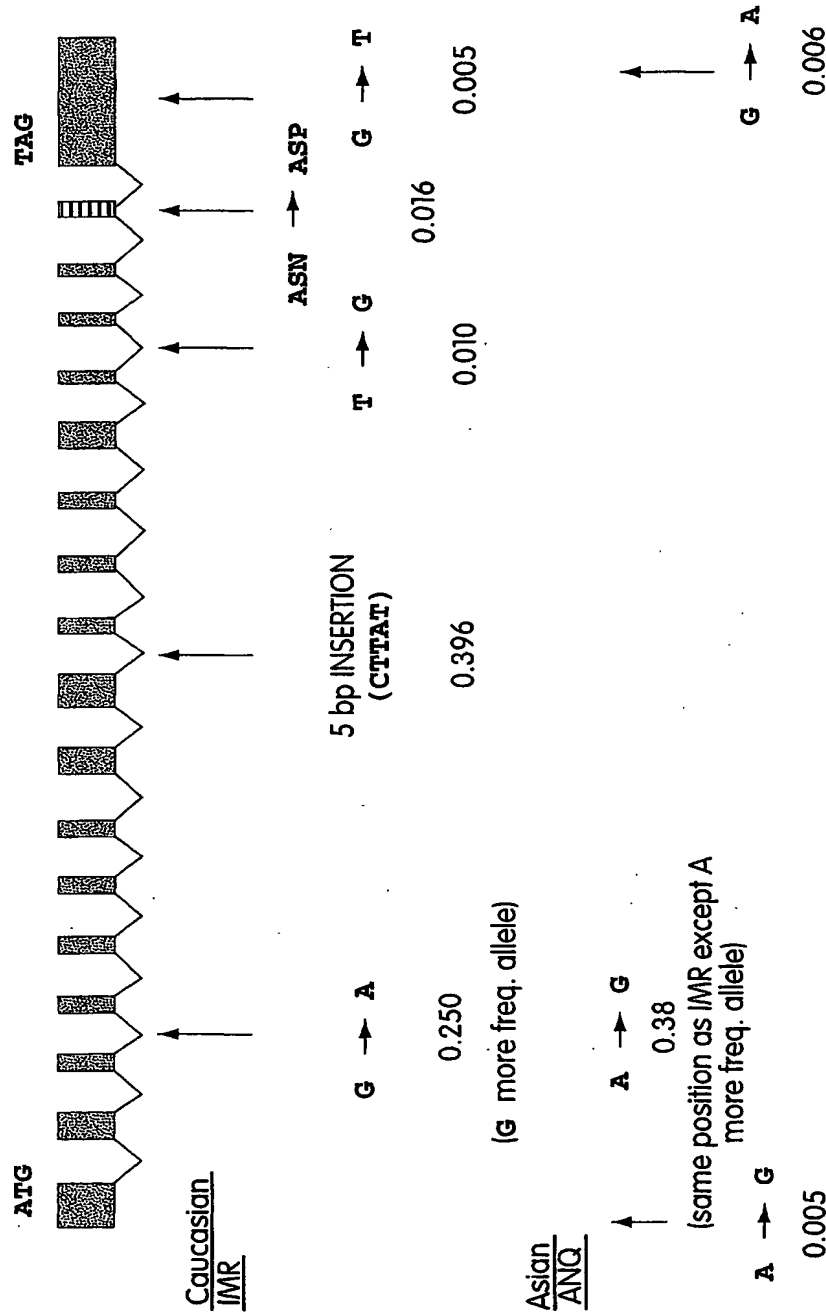


Fig. 13A

23/23

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A-G INTRONIC
1c/1d
G-A INTRONIC
A-G INTRONIC
3a/3b
5 bp INSERTION
(CTTAT)
INTRONIC
9a/9b
T-G INTRONIC
14a/14b
A-G ASN-ASP
17c/17d
A-G 3'UTR
18c/18d
G-T 3'UTR
18e/18f

Fig. 13B